

Oath/Declaration

On December 20, 2002, applicant submitted a corrected declaration that now correctly states that the priority provisional application, Serial No. 60/177,624 was filed on January 24, 2000.

Rejection under 35 U.S.C. §103(a)

Claims 1-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 97/12630 in view of Ragab U.S. 6,346,524 and Kline U.S. 6,180,096 or WO 95/13090. The Examiner maintains that motivation to combine the references comes from Kline and WO 95/13090, which the Examiner asserts, show the stabilization of interferon alpha using PEG and the formation of long-acting interferon using PEG.

In response, applicant provides the following comments. Applicant maintains its previous arguments that the prima facie case of obviousness has not been established in this case (Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) and MPEP § 2144, see response to office action, dated May 22, 2002) and that impermissible hindsight reconstruction (In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600, see response to office action, dated October 22, 2002)), has been applied to render these claims obvious.

Applicant traverses the rejection and provides the following comments. Applicant respectfully maintains that the combination of references cited by the Examiner, WO 97/12630 in view of Ragab U.S. 6,346,524 and Kline U.S. 6,180,096 or WO 95/13090, do not contain the proper motivation to render the present invention obvious. Applicant maintains that none of the references, either alone or in combination, teaches applicant's invention, a synergistic method of treatment using therapeutically effective amounts of temozolomide in combination with pegylated interferon alpha. It is maintained that the Examiner still fails to point out to the applicant, where in Ragab, WO 97/12630, Kline or WO 95/13090, a specific teaching to provide one of ordinary skill in the art the motivation to make obvious the claimed invention.

Applicant cites In re Burt, 356 F.2d 115, 121, 148 U.S.P.Q. 548, ____ (C.C.P.A. 1966), that "[s]ilence in a reference is hardly a proper substitute for an

adequate disclosure of facts from which a conclusion of obviousness may justifiably follow." Applicant respectfully maintains the cited references are silent on the applicant's claimed method of treatment, and that they do not provide one of ordinary skill in the art the motivation to combine them to render the claimed invention obvious. Furthermore, there is no sufficient guidance or teaching in any of the cited references that temozolomide and pegylated interferon- α can be synergistically combined to practice applicant's invention, as applicant will demonstrate below.

Applicant respectfully suggests that the Examiner's objection is based on an obvious to try rationale that is to "vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result . . . where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." In re O'Farrell, 853 F.2d 894, 903, 7 U.S.P.Q.2d 1637 1681 (Fed. Cir. 1988) (Citations omitted). Applicant respectfully suggests that the cited prior art have been combined to the point where, rather generally, a method of combination therapy of pegylated interferon alpha and temozolomide has been arrived at. Unlike the cited prior art, applicant provides precise dose levels of pegylated interferon alpha to be administered together with temozolomide. (See, specification, page 6, line 29 to page 7, line 12; and claims 3-5, 8-13, and 15-19). Further, applicant's specification provides a detailed clinical study design for use with the claimed method, including parameters such as patient inclusion/exclusion criteria (pages 9-12), dose escalation/de-escalation schedules and dose limiting toxicity parameters (page 13), dose adjustment of temozolomide and peg-interferon alpha (page 19), and so forth throughout the remainder of the specification. Again, applicant points out that the cited references are silent on these matters. None of the cited references suggest, let alone provide such detailed guidance to one of ordinary skill in the art to administer pegylated interferon alpha in combination with temozolomide.

Therefore, reconsideration and withdrawal of this ground of rejection is respectfully urged.

In view of the foregoing, applicant submits that the application, as pending, is in condition for allowance and courteously solicit a Notice of Allowance.

In re Application of: Sara L. Zaknoen
Serial No.: 09/767,424
Filed: January 22, 2001

No fees, other than the fee required to pay for an RCE, are believed to be due with this amendment. If any fees are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from Account No. 19-0365.

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Respectfully submitted,



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William Lee 2/26/2003
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